



US005994515A

United States Patent [19]**Hoxie**[11] **Patent Number:** **5,994,515**[45] **Date of Patent:** **Nov. 30, 1999**

[54] **ANTIBODIES DIRECTED AGAINST CELLULAR CORECEPTORS FOR HUMAN IMMUNODEFICIENCY VIRUS AND METHODS OF USING THE SAME**

[75] Inventor: **James A. Hoxie**, Berwyn, Pa.

[73] Assignee: **Trustees of the University of Pennsylvania**, Philadelphia, Pa.

[21] Appl. No.: **08/882,435**

[22] Filed: **Jun. 25, 1997**

Related U.S. Application Data

[60] Provisional application No. 60/020,396, Jun. 25, 1996, and provisional application No. 60/020,647, Jun. 27, 1996.

[51] Int. Cl.⁶ **C07K 16/28**

[52] U.S. Cl. **530/388.22; 530/387.1; 530/389.1; 424/143.1; 424/144.1**

[58] Field of Search **530/387.1, 388.1, 530/388.15, 388.21, 388.22, 388.3, 388.35, 389.1; 424/131.1, 137.1, 141.1, 142.1, 143.1, 144.1**

[56] **References Cited**
PUBLICATIONS

Hoxie, et al. : Biological characterization of a Simian . . . : J. Vir. : pp. 2557-2568, Aug. 1988.
Feng, et al. : HIV-1 Entry Cofactor: functional cDNA . . . : Science: vol. 272: pp. 872-877, May 1996.
Cohen: Likely HIV cofactor Found: Science: vol. 272: pp. 809-810, May 1996.
Alkhatib et al., 1996, *Science* 272:1955-1958.
Berson et al., 1996, *J. Virol.* 70:6288-6295.
Bleul et al., 1996, *Nature* 282:829-833.
Bleul et al., 1997, *Proc. Natl. Acad. Sci. USA* 94:1925-1930.
Brass et al., 1994, *J. Biol. Chem.* 269:2943-2952.
Brelot et al., 1997, *J. Virol.* 71:4744-4751.
Burton et al., 1994, *Adv. Immunol.* 57:191-280.
Chaudhuri et al., 1994, *J. Biol. Chem.* 269:7835-7838.
Chesebro et al., 1990, *J. Virol.* 64:215-221.
Choe et al., 1996, *Cell* 85:1135-1148.
Clackson et al., 1991, *Nature* 352:624.
Clapham et al., 1992, *J. Virol.* 66:3531-3537.
Clapham, 1991, *Rev. in Med. Virol.* 1:51-58.
Clapham et al., 1991, *Virology* 181:703-715.
Clapham et al., 1987, *Virology* 158:44-51.
Cocchi et al., 1995, *Science* 270:1811-1815.
Cohen, 1996, *Science* vol. 272:809-810.
Collins, "Scientists make AIDS breakthrough", *The Philadelphia Inquirer* (Jun. 20, 1996 ed.).
Crise et al., 1990, *J. Virol.* 64:5585-5593.
Deng et al., 1996, *Nature* 381:661-666.
Doranz et al., 1996, *Cell* 85:1149-1158.
Dragic et al., 1996, *Nature* 381:667-673.
Dragic et al., 1995, *J. Virol.* 69:1013-1018.
D'Souza et al., 1996, "Chemokines and HIV-1 second receptors", *Nature Medicine* 2:1293-1300.
Earl et al., 1994, *J. Virol.* 68:3015-3026.
Endres et al., 1996, "CD4-Independent Infection by HIV-2 Is Mediated by Fusin CXCR4", *Cell* 87:745-756.
Fahey et al., 1992, *Clin. exp. Immunol.*, 88: 1-5.

Fauci et al., 1996, *Nature* 384:529-534.

Feng et al., 1996, "HIV-1 Entry Cofactor: Functional cDNA Cloning of a Seven-Transmembrane, G Protein-Coupled Receptor", *Science* 272:872-876.

Fox 1994, No Winners Against AIDS, *Bio/Technology*, vol. 12: p. 128.

Harlow et al. 1988, In: *Antibodies, A Laboratory Manual*, Cold Spring Harbor, NY—too voluminous to submit.

Harouse et al., 1991, *Science* 253:320-323.

Haynes et al., 1996, The Finnish Medical Society DUO-DECIM, *Ann Med'* 28:39-41.

Hesselgesser et al., 1997, "CD-4-independent association between HIV-1 gp 120 and CXCR4: functional chemokine receptors are expressed in human neurons", *Current Biology* 7:112-121.

Hoxie et al., 1988, *J. Virol.* 62:2557-2568.

Hoxie et al., 1986, *Science* 234:1123-1127.

Ikeuchi et al., 1990, *J. Virol.* 64:226-4231.

Jonker et al., 1993, "In vivo treatment with a monoclonal chimeric anti-CD4 antibody results in prolonged depletion of circulating CD4+ cells in chimpanzees", *Clin. Exp. Immunol.* 93:301-307.

Koot et al., 1992, *AIDS* 6:49-54.

LaBranche et al., 1994, *J. Virol.* 68:5509-5522.

Lapham et al., 1996, *Science* 274:602-605.

Leung et al., 1994, "Chimerization of LL2, a Rapidly Internalizing Antibody Specific for B Cell Lymphoma", *Hybridoma* 13:469-476.

Li et al., 1990, *J. Virol.* 64:1383-1387.

LoBuglio et al., 1989, "Mouse/human chimeric monoclonal antibody inman: Kinetics and immune response". *Proc. Natl. Acad. Sci. USA* 86:4220-4224.

Lu et al., 1997, *Proc. Natl. Acad. Sci. USA*, vol. 94:6426-6431.

Maddon et al., 1986, *Cell* 47:333-348.

McDougal et al., 1986, *Science* 231:382-385.

McKnight et al., 1997 "Inhibition of Human Immunodeficiency Virus Fusion by a Monoclonal Antibody to a Coreceptor (CXCR4) is both Cell Type and Virus Strain Dependent", *J. Virol.* 71:1692-1696.

McKnight et al., 1996, *J. Virol.* 70:4598-4606.

McKnight et al., 1995, *J. Virol.* 69:3167-3170.

McKnight et al., 1994, *Virology*, 201:8-18.

Miyoshi et al., 1981 *Nature*, 294:770-771.

Moore, 1997, *Science* 276:51.

Nara et al., 1988, *Nature* 332:469-470.

Nara et al., 1987, *AIDS Res. and Hum. Retroviruses* 3:283-202.

Neote et al., 1993, *Cell* 72:415-425.

Oberlin et al., 1996, *Nature* 382:833-835.

Pelchen-Matthews et al., 1989, *EMBO J.* 8:3641-3649.

Picard et al., 1997, *Virology*, 231:105-111.

(List continued on next page.)

Primary Examiner—Robert D. Budens
Attorney, Agent, or Firm—Akin, Gump, Strauss, Hauer & Feld, L.L.P.

[57] **ABSTRACT**

The invention relates to an anti-immunodeficiency virus antibody which binds to a cellular protein and diagnostic and therapeutic methods of using the same.

9 Claims, 14 Drawing Sheets